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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JOHAN H GEERKE and STEVEN F. STONE

Appeal 2008-4075
Application 09/324,343
Technology Center 1600

Decided: September 24, 2008

Before DONALD E. ADAMS, LORA M. GREEN, and FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to methods of making three-layer capsule-shaped tablets. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF THE CASE

Osmotic dosage forms for drug delivery consist of an "internal compartment containing at least one drug-containing layer, at least one expandable polymer-containing layer and, optionally, one or more drug-free layers to produce a desired release pattern such as delayed or pulse release" (Spec. 2). The internal compartment "is surrounded by a membrane that is at least partially semipermeable and at least one delivery port is formed through the membrane at an appropriate location to permit release of drug-containing formulation from within the compartment" (*id.*).

The expandable polymer layer "is known as a 'push' layer because, following oral administration, fluid is imbibed through the semipermeable membrane causing the drug-containing layer(s) and any optional drug-free layer(s) to form a dispensable formulation and causing the polymer layer to expand and 'push' the dispensable formulation through the delivery port" (*id.*). Because of the importance of the delivery port's location, a colorant is used to distinguish the different layers from each other, thereby allowing drilling of the appropriate portion of the tablet, usually by laser, to produce the delivery port (*id.* at 3).

The Specification discloses "methods of making multi-layer capsule-shaped osmotic tablets having an appropriate color scheme to facilitate determination of the tablet formulation orientation by color detection at a spot location on the side of the tablet" (*id.* at 4).

Claims 18-20, 32, 33, 35, and 36 stand rejected and are on appeal (App. Br. 2-3).[1] Claims 18 and 20, the appealed independent claims, are representative and read as follows:

> 18. A method of making a three-layer capsule-shaped tablet comprising:
>
> formulating a first layer containing a drug ingredient and a second layer containing a drug ingredient, wherein one of the layers comprises a first colorant;
>
> formulating a non-drug ingredient containing third layer comprising a second colorant that is distinguishable from the first colorant or from no color and not containing any drug ingredient;
>
> compressing the first, second and third layers into a capsule-shaped osmotic tablet wherein the first layer is located at one end of the capsule-shaped osmotic tablet and the third layer is located at the other end of the capsule-shaped osmotic tablet and the second layer is located between the first layer and the third layer such that the formulation orientation of the tablet can be determined by detecting the color at a spot location on a side of the tablet corresponding to one or another differently-colored layer depending on the formulation orientation of the tablet; and
>
> detecting the formulation orientation of the tablet with a color detector directed at a spot location on the side of the tablet.
>
> 20. A method of making a three-layer capsule-shaped tablet comprising:

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[1] Appellants state that the appeal has been withdrawn with respect to claim 38 (App. Br. 2-3). When prosecution resumes in this case the Examiner and Appellants should work together to ensure that claim 38 is canceled. *See Ex Parte Ghuman,* http://www.uspto.gov/web/offices/dcom/bpai/prec/rm081175.pdf, slip op. at 5-6 (Bd. Pat. App. & Int. May 1, 2008) (precedential).

formulating a first layer containing a drug ingredient and not containing any colorant;

formulating a second layer containing a drug ingredient and a first colorant, the first colorant being complementary to no color;

formulating a third layer containing a second colorant that is distinguishable from the first colorant or from no color and not containing any drug ingredient;

compressing the first, second and third layers into a capsule-shaped osmotic tablet the first layer is located at one end of the capsule-shaped osmotic tablet and the third layer is located at the other end of the capsule-shaped osmotic tablet and the second layer is located between the first layer and the third layer such that the formulation orientation of the tablet can be determined by detecting the color at a spot location on a side of the tablet corresponding to one or another differently-colored layer depending on the formulation orientation of the tablet; and

detecting the formulation orientation of the tablet with a color detector directed at a spot location in the side of the tablet.

The Examiner cites the following documents as evidence of unpatentability:

Barclay	US 5,248,310	Sep. 28, 1993
Riddle	US 5,294,770	Mar. 15, 1994
Wong	US 5,785,994	Jul. 28, 1998

OBVIOUSNESS

ISSUE

Claims 18-20, 32, 33, 35, and 36 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Barclay in view of Wong and Riddle (Ans. 3-8).

The Examiner cites Barclay as disclosing two-layered osmotic tablets having separate polymer and drug-containing layers that are distinguishable from each other by a coloring agent in the non-drug polymer-containing

layer (Ans. 4). The Examiner states that Barclay "compresses the drug and non-drug layer together and coats the resultant solid osmotic tablet with a translucent coating" (*id.* (citing Barclay, col. 17, ll. 39-51)), a hole being then drilled through the coating to the drug-containing layer of the tablet to allow release of the drug from the capsule (Ans. 5).

The Examiner contends that Barclay differs from the claims in that "Barclay only fails to explicitly teach a three-layered tablet and further use a color detector to orient the tablet formulations" (*id.*). The Examiner cites Wong and Riddle "to show the general knowledge in the art to make a three layer tablet or use a color detector to orient tablet formulations during their manufacturing process" (*id*).

Specifically, the Examiner cites Wong as disclosing a "three or more layered tablet that provides a varying pattern of drug release . . . . Such pattern is achieved by drug concentrations in each layer of Wong's formulation. Wong et al. disclose that their tablets are prepared by pressing the three layers to form a solid core" (*id.* at 5-6). The Examiner further contends that Wong's tablets have "three layers wherein [the] first layer is drug free and is a push layer which contains a colorant such as ferric oxide . . . and the third layer comprise a colorant . . . . Thus, adding additional drug layers is well within the scope of Wong's teachings" (*id.* at 6 (citations omitted)).

The Examiner further contends that "[t]he only difference between Barclay and Wong is that Barclay teaches a two layer osmotic tablet, but Wong teaches a three layer osmotic tablet. Nevertheless, their combined teachings do not explicitly teach the use of a color detector during their manufacturing process" (*id.* at 7). The Examiner cites Riddle as disclosing

the use of a color detector to aid in drilling the access port in the coating of tablets of the type disclosed by Barclay and Wong (*id.*).

Based on these teachings, the Examiner concludes:

> [I]t would have been obvious to one ordinary skilled in the art at the time of invention to employ Barclay's method of detecting different layers in the three layer osmotic dosage forms of Wong, by incorporating a coloring agent, as shown by Barclay, in any desired layer, because the ordinary skill in the art would have had a reasonable expectation of success to use different colorants to facilitate ease of detection of each formulation layer and even further employ a color detector such as those described by Riddle to differentiate the orientation of at the tablets during their manufacturing process for any suitable step such as creating a delivery port.

(Ans. 8).

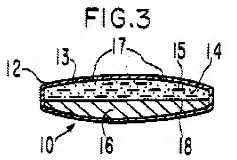
Appellants contend that the Examiner has failed to establish a prima facie case of obviousness "because combination of the respective teachings of the cited patents, even if motivated, would not have produced any claimed invention" (App. Br. 3). Specifically, Appellants argue that the capsule-shaped osmotic dosage forms produced by the methods recited in independent claims 18 and 20 have a "drug/drug/no drug orientation" which is neither taught nor suggested by the cited prior art (*id.*). Appellants further argue that the Examiner's contention, that the claimed methods would have been within the skill in the art, is insufficient to establish a prima facie case of obviousness "[b]ecause the Examiner failed to identify any objective evidence that it would have been obvious (or even possible) to modify the teachings of the prior art in a way that would have produced the three-layer, drug/drug/no drug orientation of the present invention" (*id.* at 6).

The issue with respect to this rejection, then, is whether the Examiner has made a prima facie case that one of ordinary skill in the art would have considered claims 18-20, 32-33, 35, and 36 obvious in view of Barclay, Wong, and Riddle.

FINDINGS OF FACT

1. Barclay discloses "an osmotic device for the controlled delivery of a beneficial agent to the oral cavity of an animal, and in particular a human, for an extended period of time" (Barclay, col. 4, ll. 4-6).

2. Figure 3 of Barclay, reproduced below, shows "a side sectional view of the osmotic device" (Barclay, col. 5, l. 59):



The figure shows device 10, which is "comprised of a wall **12** that surrounds and forms a compartment **13** . . . . Compartment **13** comprises a layer of a beneficial agent, identified by dots **14**, that can be from insoluble to very soluble in an exterior aqueous fluid, indicated by dashes **15**" (Barclay, col. 6, ll. 16-21). Barclay discloses:

> Compartment **13** further houses a layer of an expandable driving member **16** composed of a hydrophilic polymer, optionally cross-linked, which possesses osmotic properties such as the ability to imbibe external fluid and exhibit an osmotic pressure gradient across the wall **12** against the fluid. Wall **12** is substantially impermeable to the passage of the

> hydrophilic polymer in driving layer **16**. Layer **16** absorbs fluid imbibed into the compartment and swells.

(*Id.* at col. 6, ll. 40-48.)

3. Barclay discloses that, driven by the expanding polymer layer 16, device 10 "releases agent **14** through one or more passageways **17** in wall **12** that communicates agent **14** with the exterior of device **10**" (Barclay, col. 7, ll. 1-3).

4. Barclay discloses an example of producing the osmotic dosage form by preparing a white-colored drug-containing layer, and a reddish-brown-colored hydrophilic polymer-containing layer colored with ferric oxide, and pressing the two layers together in a tableting machine (Barclay, col. 17, ll. 20-40 (Example 2)). Barclay discloses that "[t] he hydrophilic polymer layer had a reddish-brown color, due to the ferric oxide, providing a good color contrast with the white drug-containing layer (*id.* at col. 17, ll. 40-43). The two-layered tablet is then coated with a semipermeable wall through which a single osmotic passageway is drilled into the drug-containing layer (*id.* at col. 17, ll. 43-57).

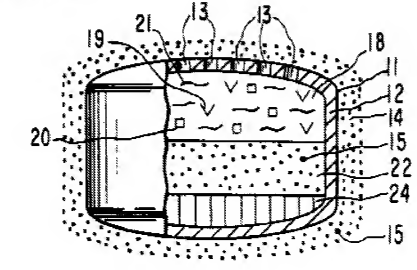
5. Barclay does not disclose an osmotic dosage form having two drug layers immediately adjacent to each other, with a non-drug layer at one end of the dosage form, and one of the two drug layers at the other end.

6. Wong discloses "a dosage form provided as an osmotic device comprising means for the rate-programmed delivery of a drug in time-varying patterns to a drug recipient" (Wong, col. 1, ll. 18-20). In one embodiment, Wong's dosage form "delivers a first or instant dose of drug at bed-time for providing drug during sleep, and a second or delayed drug early in the morning for providing drug therapy on awakening from sleep" (*id.* at

col. 2, ll. 37-40). Wong discloses that administering such a dosage at bedtime is suitable for treating high blood pressure, because of the rise in blood pressure that occurs upon waking (*id.* at col. 1, ll. 46-56).

7. Figure 4 of Wong, reproduced below, depicts "a dosage form manufactured as a programmable dosage form that provides time-varying patterns of drug delivery including drug-free intervals between drug doses of various drug-release durations including instant drug delivery and prolonged drug delivery with the latter delivered through a multiplicity of exit passageways" (Wong, col. 3, ll. 7-13):

FIG.4



Wong describes the outer components of the dosage form shown in Figure 4 as follows:

> Coat **14** provides instant drug therapy, as film coat **14** dissolves or undergoes dissolution in the presence of fluid and concurrently therewith delivers drug **15** to drug receptor. Coat **14** comprising drug **15** provides (1) instant drug followed by a drug-free interval, and (2) it essentially overcomes the time

> required for drug **15** to be delivered from the interior of dosage form **10**.

(Wong, col. 3, ll. 54-60.)

Figure 4 also shows wall 12, which is permeable to an exterior fluid but not to the drug contained within the compartment (*id.* at col. 4, ll. 19-60), with a multiplicity of passageways 13, that allow the drug 15 within the capsule to exit (*id.* at col. 13, l. 64 through col. 14., l. 6).

8. Wong discloses that the inner components of the dosage form shown in Figure 4, include "[l]ayer **18** [which] is drug-free. Layer **18** . . . provides a drug-free interval between drug **15** delivered from outside coat **14** and drug delivered from inside compartment **17**" (Wong, col. 5, ll. 24-27). Wong states that the drug-free first layer 18 "comprises a member selected from the group consisting of an osmagent **19**, represented by V, and an osmopolymer **20**, represented by squares. First layer **18** optionally comprises a binder **21** represented by wavy lines" (*id.*, col. 5, ll. 28-32).

9. Wong discloses that the inner components of the dosage form shown in Figure 4 also include "[d]rug layer **22** [which] comprises a drug **15**, represented by dots" (Wong, col. 9, ll. 39-40), and which also can contain suitable drug carriers (*id.* at col. 12, ll. 1-39).

10. Wong discloses that the inner compartment of the dosage form shown in Figure 4 also has "a third layer **24** or push layer" (Wong, col. 12, l. 40), described as follows:

> The push third layer **24** comprises an osmopolymer suitable for forming the third osmotic push layer **24**. The third layer comprises an osmopolymer that exhibits fluid imbibition properties. The osmopolymers are swellable, hydrophilic polymers which osmopolymers interact with water and aqueous biological fluids and swell or expand to an equilibrium state.

> The osmopolymers exhibit the ability to swell in water and retain a significant portion of the imbibed water within the polymer structure. The osmopolymers swell or expand to a very high degree, usually exhibiting a 2 to 60 fold volume increase.

(Wong, col. 12, ll. 41-51)

11. Wong discloses an example of preparing the osmotic dosage form by preparing a drug-free layer, a drug-containing layer, and a polymeric push layer containing ferric oxide, and pressing the three layers onto each other with a tableting die (Wong, col. 19, l. 54, through col. 20, l. 38). The three-layered tablet is then coated with a semipermeable wall through which a single drug exit port is drilled into the drug-containing layer (*id.* at col. 20, ll. 38-53). A quick release composition containing the same drug contained within the osmotic compartment is then coated onto and compressed around the semipermeable wall (*id.* at col. 20, ll. 54-64.)

12. Wong does not disclose an osmotic dosage form having two drug layers immediately adjacent to each other, with a non-drug layer at one end of the dosage form, and one of the two drug layers at the other end.

13. Neither Barclay nor Wong explicitly discloses detecting the formulation orientation of the disclosed osmotic dosage forms with a color detector.

14. Riddle discloses an apparatus for "laser drilling for forming drug release ports in pharmaceutical tablets" (Riddle, col. 1, ll. 6-8). Riddle discloses that its device is capable of distinguishing between the differently colored layers of a two layer osmotic tablet to drill drug release ports in the correct, i.e. drug-containing, side of the tablet (*id.* at col. 7, ll. 11-33).

15. Riddle does not disclose an osmotic dosage form having two drug layers immediately adjacent to each other, with a non-drug layer at one end of the dosage form, and one of the two drug layers at the other end.

PRINCIPLES OF LAW

"In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art." *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992). "[O]bviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)).

Emphasizing a flexible approach to the obviousness question, the Supreme Court has nonetheless similarly noted that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements *in the way the claimed new invention does* . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (emphasis added); *see also id.* at 1740-41 (requiring a determination of "whether there was an apparent reason to combine the known elements *in the fashion claimed* by the patent at issue") (emphasis added).

ANALYSIS

We agree with Appellants that the Examiner has not made a prima facie case that one of ordinary skill in the art would have considered claims 18-20, 32, 33, 35, and 36 obvious in view of Barclay, Wong, and Riddle.

Independent claims 18 and 20 both recite the step of "compressing the first, second, and third layers into a capsule-shaped osmotic tablet" such that "the first [(drug-containing)] layer is located at one end of the capsule-shaped osmotic tablet and the third [(non-drug-containing)] layer is located at the other end of the capsule-shaped osmotic tablet and the second [(drug-containing)] layer is located between the first layer and the third layer." Thus, as Appellants argue, claims 18 and 20 both require preparation of an osmotic dosage form that has a "drug/drug/no drug" orientation (App. Br. 3).

In contrast, Barclay discloses an osmotic tablet that contains only a single drug layer and a single non-drug layer (*see* FF 2-4). Barclay therefore differs from the claims in that Barclay's dosage form does not contain two drug layers adjacent to each other.

While Wong discloses a formulation that has two drug-containing layers (FF 6, 7), only one of those layers (22) is compressed into the osmotic dosage form, the other drug layer being coated about the entire exterior of the dosage form on the semipermeable layer (FF 7-9). Also, the interior compartment of Wong's osmotic dosage form contains a non-drug layer (18) between the outer drug coating and the drug-containing layer (FF 7, 8). Thus, the interior compartment of Wong's osmotic dosage form contains a drug layer (22) that lies between the non-drug push layer (24) at one end of the compartment, and the non-drug layer (18) adjacent to the exit port at the other end of the compartment (FF 7, 9-11).

The Examiner has not explained why Wong's disclosure of a dosage form having two drugs separated by a non-drug layer, with one of the drugs being coated outside the entire osmotic compartment, would have prompted one of ordinary skill in the art to place an additional drug-containing layer

adjacent to the drug layer of Barclay's osmotic dosage form. Nor has the Examiner explained how Barclay's disclosure of a single drug-containing osmotic dosage form would have prompted one of ordinary skill to eliminate the non-drug layer separating the two medicaments in Wong's dosage form, and replace it with a drug containing layer to achieve the orientation of the product made in independent claims 18 and 20.

Instead, the Examiner's sole rationale for modifying the prior art processes to arrive at the claimed processes is that "preparing a two or three layer osmotic tablet and using a color detector to orient a tablet are well within the level of an ordinary skill in the art," as evidenced by Wong and Riddle, which, respectively, "show the general knowledge in the art to make a three layer tablet or use a color detector to orient tablet formulations during their manufacturing process" (Ans. 5; *see also* 8-9).

However, as discussed above, neither Wong nor Riddle discloses that it was desirable to include two drug layers adjacent to each other in an osmotic dosage form. Rather, in embodiments that use two drugs, Wong discloses the desirability of providing a two-phase drug dosage by including one drug layer within the osmotic compartment and the other drug layer coating the entire outside of the osmotic compartment, the two layers being separated by a non-drug layer (FF 7-11).

The Examiner simply has not explained how an osmotic dosage form configured in the manner disclosed in Wong would have prompted one of ordinary skill in the art to prepare an osmotic dosage form by "compressing the first, second, and third layers into a capsule-shaped osmotic tablet" such that "the first [(drug-containing)] layer is located at one end of the capsule-shaped osmotic tablet and the third [(non-drug-containing)] layer is located

at the other end of the capsule-shaped osmotic tablet and the second [(drug-containing)] layer is located between the first layer and the third layer," as recited in independent claims 18 and 20.

As the Supreme Court has pointed out, "[r]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, *there must be some articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *KSR*, 127 S. Ct. at 1741 (quoting *In re Kahn*, 441 F.3d 977, 988, (Fed. Cir. 2006) (emphasis added). We agree with Appellants that, by simply averring to the general knowledge of one of ordinary skill in the art, without any supporting rationale based on the prior art or scientific reasoning, the Examiner has failed to provide the rational underpinning required to support a prima facie case of obviousness.

Thus, because the Examiner has failed to provide sound scientific reasons or specific evidence as to why one of ordinary skill in the art viewing these references would have placed two drug layers immediately adjacent to each other in an osmotic tablet in the configuration required by independent claims 18 and 20, we are compelled to reverse the Examiner's obviousness rejection of those claims and their dependents.

SUMMARY

We reverse the Examiner's rejection of claims 18-20, 32, 33, 35, and 36 under 35 U.S.C. § 103(a) as being unpatentable over Barclay in view of Wong and Riddle.

REVERSED

Ssc:

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